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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,517	09/16/2003	Sang Yup Lee	Q77445	2292

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/662,517	LEE ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claim 1 is objected to because of the following informalities: cysteine is misspelled on line 2. Appropriate correction is required.

Claim 10 is objected to because of the following informalities: a space is missing following the word plasmid on line 2. Appropriate correction is required.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-14 are unclear in the recitation of "foreign protein" as it is unclear what characteristics make a protein "foreign". While for claims 1-6, 9 and 11-14 it is presumed that this term means foreign to the bacterium recited in the claim (i.e., not endogenously produced by said bacterium), this phrase is particularly unclear as it is used within claim 7 (upon which claims 8 and 10 depend) as no bacterium is recited in claim 7. For purposes of claim 7 a "foreign protein" will be interpreted to be any protein distinct from cysteine synthase.

Claim 10 is further confusing in the recitation of a "vector according to claim 7, which is selected from plasmid pAC104CysK or plasmid pEDIL-12p40" as neither of these plasmids has the limitations recited in the vector of claim 7. Claim 7

recites a vector comprising a *cysK* gene (lacking in pEDIL-12p40) **and** a gene encoding a foreign protein (lacking in pAC104CysK). For purposes of further examination claim 10 will be examined as if it were not dependent on claim 7, i.e., A vector selected from the group consisting of plasmid pAC104CysK and plasmid pEDIL-12p40.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel vectors. Since the vectors are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmids' sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. ɔ 112 may be satisfied by a deposit of the plasmids. The specification does not disclose a repeatable process to obtain the vectors and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a

deposit of these plasmids should have been made in accordance with 37 CFR 1.801-1.809.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be available to the public under the conditions specified in 37 CFR 1.808, would satisfy the deposit requirement made herein.

If the deposit is not made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;
2. upon granting of the patent the strain will be available to the public under the conditions specified in 37 CFR 1.808;
3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
4. the deposit will be replaced if it should ever become inviable.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 4-6 rejected under 35 U.S.C. 102(b) as being anticipated by Jeong et al. (1999) or Martens et al.

Jeong et al. teach the expression of human leptin in *E.coli*. As *E.coli* endogenously contain a *cysK* gene, and leptin is a serine-rich protein, Jeong et al. meets all limitations of the instant claims.

Martens et al. teach the expression of porcine IL-12 p40 subunit in *E.coli*. As *E.coli* endogenously contain a *cysK* gene, and IL-12 p40 is a serine-rich protein, Martens et al. meets all limitations of the instant claims.

Claims 7-9 are rejected under 35 U.S.C. 102(e) as being anticipated by Seibelt et al. (WO 03/006666).

Seibelt et al. teach *E.coli* transformed with an *E.coli cysK* gene and a heterologous gene such as the *Corynebacterium glutamicum* pyruvate carboxylase gene or the *Corynebacterium glutamicum thrE* gene. A skilled artisan would understand that the genes could be provided either together on a single plasmid (Claims 7 and 8) or separately on individual plasmids (Claim 9). As such Seibelt et al. anticipate the instant claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at

> the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramirez et al. and Lamouse-Smith et al. in view of Martens et al., Swiss-Prot Accession No. P29460, Hatamoto et al. (JP 09/009982) and Koonin et al.

Ramirez et al. and Lamouse-Smith et al. teach that recombinant protein production in *E. coli* can be improved by increasing the available levels of amino acids present in the recombinant protein in levels substantially above the levels of that amino acid in *E. coli* proteins. Lamouse-Smith et al. specifically teach that serine-family amino acids in particular are often present in higher levels in recombinant proteins and that the metabolic burden imposed by amino acid composition can be alleviated by supplementing the cell with required precursors.

Martens et al. teach the usefulness of IL-12 p40 as an IL-12 antagonist for the treatment of septic shock and other conditions and the recombinant production of high levels of this protein in *E. coli*.

Swiss-Prot Accession No. P29460 teaches the amino acid sequence of human IL-12 p40 showing that this protein has 3.3% cysteine residues.

Koonin et al. teach the average amino acid composition of *E. coli* proteins (see Table 1) and specifically that on average *E. coli* proteins have only 1.1% cysteine residues.

Hamamoto et al. teach methods of increasing the amount of cysteine produced in *E.coli* comprising transforming *E. coli* with a plasmid encoding the *E.coli* genes for *cysE*, *cysK* and *pta* and teach a vector encoding these genes (see the enclosed English abstract of Hamamoto et al.). Applicants should note that a complete English translation of Hamamoto et al. has been requested and will be provided as soon as it is recieved.

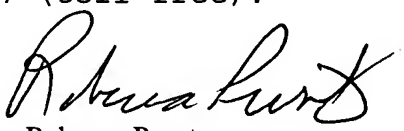
As Martens et al. teach that a skilled artisan would clearly desire to produce high levels of IL-12 p40 in *E. coli* and a comparison of Swiss-Prot Accession No. P29460 with the amino acid composition of *E. coli* proteins of Koonin et al. shows that this protein has 3 times more cysteine than the average *E. coli* protein, it would have been obvious to produce

the IL-12 p40 in an *E. coli* cell have increased levels of cysteine, such as the transformed cells of Hamamoto et al. One of skill in the art would have been motivated to use the cells of Hamamoto et al. by the disclosures of Ramirez et al. and Lamouse-Smith et al. that recombinant protein production in *E. coli* can be improved by increasing the available levels of amino acids present in the recombinant protein in levels substantially above the levels of that amino acid in *E. coli* proteins. Furthermore, one of skill in the art would have found it obvious to either include the gene encoding IL-12 p40 on the same vector as the *cysE*, *cysK* and *pta* genes of Hamamoto et al. or alternatively to include it on a separate vector.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Rebecca Prouty
Primary Examiner
Art Unit 1652